SAS Journal of Medicine ISSN 2454-5112
SAS J. Med., Volume-2; Issue-3 (May-Jun, 2016); p-64-68
Available online at http://sassociety.com/sasjm/

Case Series

Takayasu arteritis in Iran

Mohammad Hassan Jokar
Department of Internal Medicine, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

***Corresponding author**
Mohammad Hassan Jokar
Email: jokarmh@mums.ac.ir

Abstract: Takayasu arteritis is a chronic large vessel vasculitis of unknown etiology. Our aim was to describe the demographic, clinical, and laboratory features of Takayasu arteritis in northeast of Iran. We respectively studied the medical records of 38 patients with diagnosis of Takayasu arteritis at the Department and clinic of Rheumatology of the Emam Reza Hospital, Mashhad, Iran between January 1, 2005, and December 31, 2015. We used the American College of Rheumatology (ACR) classification criteria for Takayasu arteritis to classify our patients. Data's regarding to the patients, including age, sex, clinical features, laboratory and imaging findings, and type of treatment were extracted from the files. The collected data were analyzed using SPSS software (version 18). The male: female ratio was 1:18. The mean age of onset was 25.32 ± 7.01 years. The most common manifestations were: arm claudication 94.73%, bruit 84.21%, pulse deficit 84.21%, central nervous system symptoms 31.57%, fever 47.63%, weight loss 50.00%, and hypertension 68.42%. Serum C-reactive protein level (CRP) and Erythrocyte sedimentation rate (ESR) were elevated in 92.10% and 97.36% of patients respectively. The most common involved vessels were: right carotid artery 81.60%, left subclavian artery 78.94%, left carotid artery 76.30%, and right subclavian artery 73.70. Mean duration of treatment was 68.36±36.77 months. Mean cumulative prednisolone dose was 23745 mg. There was no mortality due to Takayasu arteritis in our patients.Takayasu arteritis is relatively common in northeast of Iran. The most common manifestations of Takayasu arteritis in northeast of Iran are: arm claudication, headache, vertigo, fever, weight loss, hypertension and visual abnormality.
Keywords: Takayasu disease, arteritis, vasculitis.

INTRODUCTION:

Takayasu arteritis (TA) is a chronic large vessel vasculitis of unknown etiology. TA affects adolescent girls and young women. It has a worldwide distribution, with the greatest prevalence in Asians [1, 2]. A diffuse inflammatory syndrome with anorexia, fever, night sweats, malaise, weight loss, and diffuse myalgia are often the first manifestations of TA. These symptoms are frequently misdiagnosed as an infection [3].Takayasu arteritis mainly affects the aorta and its primary branches [4]. The inflammatory processes cause thickening of the walls of the involved vessels. The proximal aorta can become dilated due to inflammatory injury. Narrowing, occlusion, or dilation of the arteries with varying degrees results in a wide variety of symptoms [3].

Carotid and vertebral arteries involvement can lead to neurologic and ophthalmologic problems, including headache, syncope, dizziness, tinnitus, stroke, and visual impairment. Jaw claudication and facial muscles atrophy are mainly late manifestations. Brachiocephalic and subclavian arteries obstructions decrease blood flow to the upper extremities and lead to arm claudication, pulselessness, and unequal arm blood pressures. The finding of arterial bruits can be helpful in making the diagnosis [5].

TA is not very rare in Iran [6, 7]. We aimed to study the clinical and laboratory characteristics, response to treatment and prognosis in our patients with diagnosis of TA.

METHODS:

In a retrospective study, we reviewed the medical records of our patients with an impression of Takayasu Arteritis at the Department of Rheumatology of Emam Reza Hospital, Mashhad, Iran during 10 years (2005- 2015). We extracted and analyzed data's regarding to the patients, including age, sex, clinical features, laboratory findings, images and type of treatment from files. Patients were classified according to the American College of Rheumatology (ACR) 1990 classification criteria for TA (8). From a total of 45 files that reviewed, 38 patients had enough criteria for diagnosis of Takayasu disease.

Statistical Analysis:

We represented continuous data as mean and standard deviation (mean ± SD), and categorical variables as a percentage. The data were analyzed using SPSS software (version 18).

RESULTS:

There were 38 patients (2 male, 36 female). The mean age at diagnosis of Takayasu arteritis was 25.32 ± 7.01 years (minimum 16 years, maximum 40 years). The clinical and laboratory features of studied patients are shown in table 1.

Laboratory findings:

Erythrocyte sedimentation rate (ESR) was elevated in 97.36% of patients (mean 71.60 mm/1st hour, minimum 18 mm/1st hour and maximum 115 mm/1st hour). Anemia (Hemoglobin level of below 12g/dl in females and below 14gr/dl in males) was present in 63.15% of patients. Leukocytosis (WBC counts> 10000/µl) was present in 26.31% of patients.

Imaging findings:

The most commonly involved arteries were: right carotid artery 81.60%, left subclavian artery 78.94%, left carotid artery 76.30%, right subclavian artery 73.70%, and renal artery 68.40%. Superior mesenteric artery was involved in 1 (2.63%) patient.

Diseases association:

Three of our patients had another inflammatory disease (SLE in 1, Antiphospholipid antibody syndrome in 1 and subacute thyroiditis in 1 patient).

Pregnancy outcome:

There were 10 pregnancies in our patients, of them 7 had successful and normal courses. Three patients had complicated pregnancy (spontaneous abortion in 1, preeclampsia and therapeutic abortion in 1 and ectopic pregnancy in 1 patient).

Treatment:

Initial dose of prednisolone was 1mg/kg/day (maximum 60 mg). Ninety seven percent of patients had received other immunosuppressive drugs (methotrexate or azathioprine).

Renal artery angioplasty has been done in 2 patients due to uncontrolled hypertension. The most common steroid side effects were: Cushing's syndrome in 38(100%) patients, cataract in 1(2.63%) patient, central serous retinopathy in 1 (2.63%) patient and pulmonary tuberculosis in 1 (2.63%) patient.

Diagnosis and Course:

The time from onset of symptoms to diagnosis ranged from two to 36 months (mean 13.57 months). There was not any mortality in our patients due to Takayasu arteritis.

Table 1: Clinical Features of Takayasu's Arteritis

Feature	At Presentation No (%)	Ever Present No (%)
Claudication (upper extremity)	25 (68.42)	36 (94.73)
Bruit	13 (34.21)	32 (84.21)
Unequal arm blood pressures	12 (31.57)	20 (52.63)
Hypertension	4 (10.42)	26 (68.42)
Carotidynia	5 (13.15)	6 (15.78)
Aortic regurgitation	1(2.63)	4 (10.42)
Lightheadedness	3 (7.89)	9 (23.68)
pulse deficit	27 (71.05)	32 (84.21)
Visual abnormality	3 (7.89)	5 (13.15)
Stroke	2 (5.26)	4 (10.42)
Headache	0 (0.00)	7 (21.28)
Seizure	1 (2.63)	1 (2.63)
Chest pain	3 (7.89)	4 (10.42)
Joint pain	4 (10.42)	15 (39.47)
Myalgia	18 (47.36)	19 (50.00)
Malaise	20 (52.63)	21 (55.26)
Fever	18 (47.63)	18 (47.63)
Weight loss	19 (50.00)	19 (50.00)
High ESR	37 (97.36)	37 (97.36)
High CRP	35 (92.10)	35 (92.10)
Anemia (Hb<12g/dl)	24 (63.15)	24 (63.15)
Leukocytosis (WBC>10000/ml)	10 (26.31)	10 (26.31)

DISCUSSION

Takayasu arteritis (TA) is a form of large vessel vasculitis. The large vessel vasculitides affect the aorta and its branches and include giant cell arteritis and Takayasu arteritis [9]. In 1908 Dr. Mikito Takayasu described the first case of Takayasu's arteritis [9]. Takayasu arteritis has become increasingly recognized as a worldwide disease with a variable spectrum of disease expressions [10-16]. Female predominance and ethnic difference are characteristics of this disease. Women are affected in 80 to 90 percent of cases [17]. In our study the male to female ratio was 1 to 18. The age of onset is usually between 10 and 40 years [17]. We found a mean age of 25.32 ± 7.01 years (minimum 16 years, maximum 40 years).

Clinical manifestations of TA range from asymptomatic disease found as a result of nonpalpable pulses or bruits, to catastrophic neurological disorder [18, 19]. Table 2 shows the frequency, clinical and laboratory features of TA in our patients. For comparison, clinical and laboratory features of TA in some other populations are shown too. The frequencies of common complaints vary between different Series. In the early phase of TA systemic symptoms are common, including low-grade fever, fatigue and weight loss [3]. About half of our patients had Systemic symptoms.

Vascular symptoms are rare at presentation [20]. As the disease progresses, however, evidence of vessel involvement and ischemia become clinically apparent, the extremities become cool, and pain develops with use (arm or leg claudication). In advanced cases, occlusion of the vessels to the extremities may result in ischemic ulcerations or gangrene [21]. Ninety percent of our patients had upper extremity claudication, but we didn't have any lower extremity claudication. None of our patients had ischemic ulcerations or gangrene in their extremities.

Arthralgias or myalgias are present in about one-half of cases. Clinically evident synovitis is less common [22]. About half of our patients had myalgia and more than 1/3 of them had arthralgia.

Involvement of the carotid and vertebral arteries can decrease cerebral blood flow, leading to symptoms such as vertigo, syncope, headaches, convulsion and dementia. Neurological involvement is not common in Takayasu disease and neurological syndromes as the first manifestation of the disease are relatively rare [23, 24]. Involvement of intracranial arteries and also of cranial nerves, as the sole, or as the first manifestation of the disease has been reported in a few case report articles [25-28]. Visual impairment is a late manifestation and is due to cerebral ischemia [29]. There were 2 cerebrovascular accidents (CVA) in our patients. TA was presented as hemiplegia in one. The other patient with CVA had antiphospholipid syndrome too. We found seizure in one of our patients. Visual symptoms were present in 13% of patients.

In physical examination arterial pulses in the upper and lower extremities are diminished and often asymmetrical. Bruits are usually audible over involved arteries. Clinical signs of aortic regurgitation may be present in patients who have this abnormality [30]. More than half of our patients had unequal arm blood pressures and 84% had Bruits. Hypertension is seen in 68% of patients as a result of narrowing of the renal arteries, or narrowing and decreased elasticity of the aorta and its branches [18]. In our study 68% of the patients had hypertension. Carotidynia (pain appearing along the carotid course) can be seen in 2-31 percent of patients [17]. Sixteen percent of our patients had carotidodynia.

Laboratory findings reflect the inflammatory process, but are mostly nonspecific [29]. A normochromic normocytic anemia suggestive of the anemia of chronic disease is present in most patients. The white blood cell count is usually normal [18]. The most common Laboratory findings in our study were: elevated ESR (97%), elevated CRP (92%), and anemia (61%).

The disease commonly is diagnosed more often with a delay in from the onset of the first symptoms of months to years. In one of the largest cohorts (n = 107) the time from onset of symptoms to diagnosis was two to 11 years [15]. In our study, the time from onset of symptoms to diagnosis ranged from two to 36 months (mean 13.57 months).

The mainstay of therapy for Takayasu arteritis is glucocorticoids. An initial daily dose of 1 mg/kg/day of prednisone should be started [30]. In glucocorticoid-resistant cases, additional therapy with methotrexate or cyclophosphamide is usually added. European League Against Rheumatism (EULAR) recommends high doses of glucocorticoids for the remission of the disease and favours an immunosuppressive agent as an adjunctive therapy [32]. All of our patients were treated with 1mg/kg/day (maximum 60 mg) prednisolone. The vast majority of our patients (97.36%) had received methotrexate or azathioprine as a corticosparing drug.

The mean duration of treatment was 68.36±36.77 months (minimum 31 months, maximum 156 months). The mean cumulative prednisolone dose was 23745 mg (minimum 4200 mg, maximum 55075 mg). TA is a chronic and progressive disease with a remitting and relapsing course along with chronic therapy of glucocorticoids. The five years survival is 88-90% [31]. There was no mortality due to Takayasu

arteritis in our patients.

Since TA affects mainly women in the reproductive ages, it is not uncommon to either find women with TA contemplating pregnancy or for the disease to be diagnosed for the first time during pregnancy itself. A good pregnancy outcome is usually reported in women with TA and the basic disease process does not seem to be affected by pregnancy. However, hypertension, aneurysm formation, Takayasu retinopathy, and aortic regurgitation may cause grievous pregnancy complications [33]. There were 10 pregnancies in our patients, of them 7 were successful. Three patients had complicated pregnancy (spontaneous abortion in 1, preeclampsia and therapeutic abortion in 1 and ectopic pregnancy in 1 patients).

TA has been associated with other inflammatory diseases [34]. Three of our patients had another inflammatory disease (SLE in 1, antiphospholipid antibody syndrome in 1 and subacute thyroiditis in 1 patients).

Table 2: Common symptoms and signs in Takayasu's arteritis

	Brazil [10] (n=73)	China[11] (n=530)	India[12] (n=106)	Japan[13] (n=52	Korea[14] (n=129)	Mexico [15] (n=107)	USA[16] (n=60)	South Iran [6] (n=20)	Northeast Iran (n=38)
Mean age (years)	27	-	27.3	-	-	-	25	27.3	25.32
M/F	1/5	1/2.9	1/1.6		1/6.6	1/8.5	1/32	1/4	1/18
Fever (%)	18 (24.65)	-	-	-	-	-	12 (20.00)	7(35.00)	18 (47.63)
Fatigue (%)	-	-	-	14 (26.92)	44 (34.10)	83 (77.57)	26 (43.33)	13(65.00)	21 (55.26)
Weight loss (%)	20 (27.39)	-	10 (9.43)	-	14 (10.85)	24 (22.42)	12 (20.00)	6(30.00)	19 (50.00)
Musculoskeletal (%)	19 (26.02)	-	5 (4.71)	3 (5.76)	-	57 (53.27)	32 (53.33)	-	-
Arm Claudication (%)	42 (57.53)	132 (24.90)	-	7 (13.46)	66 (51.16)	31 (28.97)	54 (90.00)	10(50.00)	36 (94.73)
Headache (%)	33 (45.20)	-	47 (44.33)	16 (30.76)	77 (59.68)	61 (57.00)	25 (41.66)	13(65.00)	7 (21.28)
Visual changes (%)	-	53 (10.00)	13 (12.26)	3 (5.76)	26 (20.15)	9 (8.41)	18 (30.00)	6(30.00)	5 (13.15)
Carotidynia (%)	-	-	-	11 (21.15)	3 (2.32)	-	19 (31.66)	-	6 (15.78)
Hypertension (%)	26 (35.61)	318 (60.00)	82 (77.35)	17 (32.69)	52 (40.30)	77 (71.96)	21 (35.00)	15(75.00)	26 (68.42)
Bruit (%)	47 (64.38)	307 (57.92)	37 (34.90)	-	48 (37.20)	101 (94.39)	48 (80.00)	11 (55.00)	32 (84.21)
Decreased pulses (%)	62 (84.93)	196 (36.98)	-	32 (61.53)	71 (5503)	103 (96.26)	36 (60.00)	15(75.00)	32 (84.21)
UBP* (%)	-	-	-	-	-	-	28 (46.66)	-	20 (52.63)
Elevated ESR (%)	-	-	-	-	-	-	-	8 (40.00)**	37 (97.36)
Anemia (%)	-	-	-	-	-	-	-	14 (70.00)	23 (60.52)
Leukocytosis (%)	-	-	-	-	-	-	-	9 (45.00)	9 (23.68)

* Unequal blood pressure

**ESR≥60mm/hr

- The frequency of the finding was not mentioned in the study

CONCLUSION:

Takayasu arteritis is not a rare disease in the northeast of Iran. The most common manifestations of Takayasu arteritis in northeast of Iran are: arm claudication, headache, vertigo, fever, weight loss, hypertension, visual abnormality and carotidynia.

REFERENCES

1. Dab ague J, Reyes PA; Takayasu arteritis in Mexico: a 38-year clinical perspective through literature review. Int J Cardiol. 1996; 54 Suppl: S103.
2. Hall S, Barr W, Lie JT, Stanson AW, Kazmier FJ, Hunder GG; Takayasu arteritis. A study of 32 North American patients. Medicine (Baltimore) 1985; 64:89.
3. Park MC, Lee SW, Park YB, Chung NS, Lee SK; Clinical characteristics and outcomes of Takayasu arteritis: analysis of 108 patients using standardized criteria for diagnosis, activity assessment, and angiographic classification. Scand J Rheumatol. 2005; 34(4):284-92.
4. Hata A, Noda M, Moriwaki R, Numano F; Angiographic findings of Takayasu arteritis: new classification. Int J Cardiol 1996; 54 Suppl: S155.
5. Sharma BK, Jain S, Sagar S; Systemic manifestations of Takayasu arteritis: the expanding spectrum. Int J Cardiol 1996; 54 Suppl: S149.
6. Jokar M, Mirfeizi Z; Epidemiology of Vasculitides in Khorasan Province, Iran. Iranian Journal of Medical Sciences. 2015; 40(4):362-366.
7. Rabeei M, Kashef S, Ajami GH H; Retrospective study of Takayayasu's disease in hospitalized patients of teaching hospitals of Shiraz University of medical science from 1985- 2000, (in IRAN).Canadian Journal on Chemical Engineering

& Technology. 2012; 3(1):12-21.
8. Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, *et al.;* The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 1990; 33(8):1129-34.
9. Jokar M.H, Mirfeizi Z; The Demographic, Clinical and Laboratory Profile of Patients with Giant Cell Arteritis: Case Series. Sch. J. App. Med. Sci., 2014; 2(5F):1892-1895.
10. Sato EI, Hatta FS, Levy-Neto M, Fernandes S; Demographic, clinical, and angiographic data of patients with Takayasu arteritis in Brazil. Int J Cardiol 1998; 66(Suppl. 1): S67–70.
11. Zheng D, Fan D, Liu L; Takayasu arteritis in china: a report of 530 cases. Heart Vessels 1992; 7(Suppl.): S32–6.
12. Jain S, Kumari S, Ganguly NK, Sharma BK; Current status of Takayasu arteritis in India. Int J Cardiol 1996; 54 (Suppl.): S111–6.
13. Ueda H, Morooka S, Ito I, Yamaguchi H, Takeda T; Clinical observations of 52 cases of aortitis syndrome. Jpn Heart J 1969; 10: 227–88.
14. Park YB, Hong SK, Choi KJ, Sohn DW, Oh BH, Lee MM, *et al.;* Takayasu arteritis in Korea: Clinical and angiographic features. Heart Vessels 1992; 7(Suppl.): S55–9.
15. Lupi-Herrera E, Sánchez-Torres G, Marcushamer J, Mispireta J, Horwitz S, Vela JE; Takayasu arteritis. Clinical study of 107 cases. Am Heart J 1977; 93: 94–103.
16. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M, *et al.;* Takayasu arteritis. Ann Intern Med 1994; 120: 919–29.
17. Hellmann DB; Giant Cell Arteritis, Polymyalgia Rheumatica, and Takayasu Arteritis. In: Firestein GS, Budd RC, editors. Kelley's Textbook of Rheumatology. ELSEVIER; 2015; 1322-27.
18. Langford CA; Takayasu arteritis. In: Hochberg MC, Silman AJ, Smolen OS, editors. RHEUMATOLOGY. Elsevier; 2011; 1567-1573.
19. Johnston SL, Lock RJ, Gompels MM. Takayasu arteritis: a review. J Clin Pathol 2002; 55:481–486.
20. Noris M, Daina E, Gamba S, Bonazzola S, Remuzzi G. Interleukin-6 and RANTES in Takayasu arteritis: a guide for therapeutic decisions? Circulation 1999; 100(1):55-60. PubMed PMID: 10393681.
21. Ogino H1, Matsuda H, Minatoya K, Sasaki H, Tanaka H, Matsumura Y, *et al.;* Overview of Late Outcome of Medical and Surgical Treatment for Takayasu Arteritis. Circulation 2008; 118:2738-2747.
22. Maksimowicz-McKinnon K, Clark TM, Hoffman GS; Limitations of therapy and a guarded prognosis in an American cohort of Takayasu arteritis patients. Arthritis Rheum 2007; 56:1000-1009.
23. Bradlly WG, Daroff RB, Fenichel GM, Jankovic J; Neurology in clinical practice. 4th edition. Philadelphia, Elsevier Inc; 2004; 1104-11.
24. Ureten K, Ozturk MA, Onat AM, Ozturk MH, Ozbalakan Z, Guvener M, *et al.;* Takayasu arteritis: results of a university hospital of 45 patients in Turkey. Int J Cardiol, 2004; 96 (2):259-64.
25. Ringleb PA, Strittmatter EI, Loewer M, Hartmann M, Fiebach JB, Lichy C, *et al.;* Cerebro- vascular manifestations of Takayasu arteritis in Europe. Rheumatology (Oxford), 2005; 44 (8): 1012-5.
26. Cantú C1, Pineda C, Barinagarrementeria F, Salgado P, Gurza A, Paola de Pablo, *et al.;* Noninvasive cerebrovascular assessment of Takayasu arteritis. Stroke, 2000; 31(9): 2197-202.
27. Hoffmann M1, Corr P, Robbs J; Cerebrovascular findings in Takayasu disease. J. Neuroimaging, 2000; 10(2): 84-90.
28. Sikaroodi H1, Motamedi M, Kahnooji H, Gholamrezanezhad A, Yousefi N; Stroke as the first manifestation of Takayasu arteritis. Acta neurol. Belg. 2007; 107 (1):18-21.
29. Rodríguez-Pla A1, de Miguel G, López-Contreras J, de Llobet JM, Llauger J, Díaz C; Bilateral blindness in Takayasu disease. Scand J Rheumatol 1996; 25:394.
30. Kerr GS; Takayasu arteritis. Rheum Dis Clin North Am 1995; 21:1041.
31. Al-Bishri J; Takayasu Arteritis: A Review Article. British Journal of Medicine & Medical Research, 2013: 3(4): 811-820.
32. Mukhtyar C, Guillevin L, Cid MC, Dasgupta B, de Groot K, Gross W *et al.;* EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009; 68:318–323.
33. Hauenstein E1, Frank H, Bauer JS, Schneider KT, Fischer T; Takayasu Arteritis and Pregnancy: review of literature and discussion. J Perinat Med. 2010; 38(1):55-62.
34. Ohta Y, Ohya Y, Fujii K, Tsuchihashi T, Sato K, Abe I, Iida M; Inflammatory diseases associated with Takayasu arteritis. Angiology. 2003; 54(3):339-44.